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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,806	11/16/2001	David C. Johnson	899-59399	6730

24197 7590 02/11/2004

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,806	JOHNSON ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-23,25 and 29-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-23, and 29-38* is/are rejected.

7)☒ Claim(s) *19-20,23,25, 29-31,35 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/05/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed August 09, 2001 and November 03, 2003 have been entered.

Election/Restrictions

2. Applicant's election without traverse of Group II, drawn to claims 19-23, 25, and 29-38, in Applicant's response to the restriction requirement, dated November 03, 2003 is acknowledged.

Status of Claims

3. Claims 1-38 were pending. Claims 1-18, 24, and 26-28, drawn to non-elected invention, are cancelled. Claims 19-23, 25, and 29-38 are currently under examination.

Claim Objections

4. Claim 19-20, 23, 29-31, and 35-36 are objected to because of the following informalities: The use of abbreviation, "US2". The use of abbreviation should be avoided in the claims. However, if it is necessary to use abbreviation for the sake of brevity, the abbreviation should be spelled out in the first instance of use in the claims. In addition, it appears that the US2 protein that Applicant is directing cytomegalovirus, not any other virus. If this is the case, for the purpose of clarity, Applicant is required to identify the virus where the protein originates. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is rendered indefinite for the recitation of "exogenously supplied". It is unclear what is intended by such recitation, because if the purified protein does not come from an outside source, then where else can it come from in order to practice the full scope of the claimed invention, which requires the introduction of the purified protein into a mammal.

Claim 23 is rendered indefinite for the recitation of "US2 protein biological activity". Again, it is unclear what is intended by such recitation. If Applicant intends on a specific activity such as CD4+ AND CD8+, Applicant must introduce those specific activity(ies) into the claims. Without such, the claims are rendered indefinite because it is unclear what the nature of activity that is required to fulfill the limitation expressed in the claims.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 23 is directed to amino acid sequences that have at least 70% sequence identity to residues 28-143 of SEQ ID NO: 3 or conservative amino acid substitutions of residues 28-143 of SEQ ID NO: 3.

A 30% variation of the 115 amino acid sequence is approximately 35 amino acids. However, the specification does not contains any teaching that are directed to i) any percentage of sequence identity nor does it teaches the activity, ii) function that must be present in such sequences, iii) nor does it teaches that such sequences is capable of having the same desired function. Therefore, the claim read on amino acids with no defined structure and function, and the specification does not reasonably convey possession of these undefined amino acid sequences.

8. Claims 19-22, and 29-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24

(CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wrigtht*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

The nature of the invention is directed to inhibiting recognition of cells or tissues by both CD8+ and CD4+ T cells; inhibiting a CD4+ mediated immune response; and inhibiting autoimmune, transplant, and gene therapy immune response with the introduction of a purified US2 protein or a therapeutically effective fragment thereof.

The guidance that is provided in the specification is limited to an in vitro use of a purified US2 protein to inhibit presentation of tetanus toxin to CD4+ T cells, working Example 8. Example 8 is the only working example, and guidance provided in the specification that relates to the instantly claimed invention. The example is effective in enabling the in vitro use of purified US2 protein in macrophages to block the recognition of tetanus toxin to CD4+ T cells. However, the example and the disclosure do not

commensurate with the full scope/breadth of the claims. The full scope/breadth of the claims encompasses i) all cells and tissues; ii) an in vivo use of the claimed invention in mammals, humans and non-humans; and iii) the use of the instant claimed invention to inhibit autoimmune, transplant, and gene therapy immune responses.

The MPEP does not require an in vivo working example to enable a claimed invention that is directed to an in vivo use. However, it does require that the in vitro data correlate with the intended in vivo use of the claimed invention, which is to inhibit CD4+ and CD8+ recognition of all tissues and cells, and inhibition of autoimmune, transplant, and gene therapy immune responses. In the instantly claimed invention, such correlation cannot be found. Thus, the in vitro data is not enabling for the in vivo use of the claimed invention.

Further, the specification lacks guidance and teachings such as the dosage amounts required to achieve the desired effects, course of treatment, and parameters or conditions that can be used to monitor the progression of such therapy. The specification lacks data that concerns the expression of US2 and observation of it's activity in tissues and cells, such as: epithelial, glial, endothelial cells, fibroblasts, B cells, dendritic cells, monocytes/macrophages, and many more because the prior art teaches, Chevalier et al., that HCMV can infect diverse cell types, and generally replicate slowly in most cells.

The state of the prior art teaches that MHC class I complexes, CD8+ T cells are affected by US2. However, a discrepancy emerges when it comes to the effects of US2 protein on MHC class II. Tomazin et al., Applicant, teaches that US2 destroys two

components of MHC class II pathway, therefore prevents recognition by CD4+ T cells. However, Rehm teaches that MHC class II complexes are unaffected by the US2 protein. Thus, in view of the discrepancy, it is concluded that the level of unpredictability in the art is high.

Thus, in view of the limiting scope that the working example enables, which is not directed to any aspect of the instantly claimed invention, and it's contrast to the breadth of the claims, the lack of guidance presented, the relative skill of those in the art required to practice the claimed invention is high, and the discrepancy in the teachings in the prior art, the quantity of experimentation necessary to make and use the claimed invention would be great.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Weston et al.

Claim 23 recites a purified soluble protein having US2 protein biological activity, and comprising an amino acid sequence selected from the group consisting of:

(a) residues 28-143 of SEQ ID NO: 3;

(b) amino acids sequences that differ from those specified in (a) by one or more conservative amino acid substitution; and

(c) amino acid sequences having at least 70% sequence identity to the sequences specified in (a) or (b).

Claim 25, which depends on claim 23, further limits the sequence to SEQ ID NO: 5.

Weston teaches a US2 human cytomegalovirus sequence, labeled HQLF2, that is the same as residues 28-143 of SEQ ID NO: 3, and have 78.1% identity to SEQ ID NO: 5 of the instantly claimed invention. Weston et al. does not teach a "purified soluble" protein or a sequence that has 100% identity to SEQ ID NO: 5. However, at the time of the claimed invention, it would have been obvious for one of ordinary skills in the art to use standard genetic engineering techniques, as asserted on page 28 of the specification, to produce a purified soluble US2 protein or variants thereof. One of ordinary skills in the art would have been motivated by the teaching of Weston et al. to dissect the sequence genome of cytomegalovirus as part of routine experimentation to evaluate the activity of different aspects of the genome in tissue cultures and perhaps find a use or purpose for the entire genome or certain aspects of the genome with reasonable amount of success.

11. Claims 37-38 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ploegh et al.

Ploegh et al. teach a composition and pharmaceutical composition that comprises the nucleic acids that encodes US2 protein and a pharmaceutically acceptable excipient. (See claims 22-24, and 26-28). Ploegh et al. does not teach the use of the US2 protein to make compositions and pharmaceutical compositions.

However, at the time of the claimed invention, it would have been obvious to one of ordinary skills to substitute the nucleic acid sequence taught by Ploegh with the US2 sequence or variants thereof that is taught by Weston to make a composition or pharmaceutical composition that comprises the protein. In addition, as asserted by page 28 of the specification, it would have been obvious for one of ordinary skills in the art to use "standard genetic engineering techniques" to make the composition or the pharmaceutical composition. One of ordinary skills in the art would have been motivated to take the protein that is taught by Weston to make the composition and pharmaceutical composition that is taught be Ploegh OR use standard genetic engineering to make the composition or pharmaceutical composition as part of routine experimentation to determine the best mode of delivery for the protein that is well known in the art to inhibit the MHC class I antigen presentation pathway that presents antigens to CD8+ T cells with reasonable expectation of success.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al in view of Weston.

Jones et al. teaches a US2 protein that destabilizes MHC class I. Jones does not teach the exact amino acid sequence instantly claimed.

Weston teaches the amino acid sequence of the US2 protein. However, at the time to the claimed invention, it would have been obvious to one of ordinary skills that the US2 protein taught by Jones is either the exact protein that is taught by Weston et al. or variants thereof. Thus, one would have been motivated to refer the teachings by Weston to produce the US2 protein that is taught by Jones et al. or variants thereof as part of routine experimentation to confirm the teaching of Jones et al. or to observe additional activity of the protein in various cells or immune system with reasonable expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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